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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/550,414	09/23/2005	Ryuji Ueno	278283US0X PCT	2194

22850 7590 01/26/2007

OBLON, SPIVAK, MCCLELLAND, MAIER & NEUSTADT, P.C.
1940 DUKE STREET
ALEXANDRIA, VA 22314

EXAMINER	
RAMACHANDRAN, UMAMAHESWARI	
ART UNIT	PAPER NUMBER
1617	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/26/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/550,414	UENO ET AL.	
	Examiner	Art Unit	
	Umamaheswari Ramachandran	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Restriction/Election

Applicant's election of group II claims 1-10 in the reply filed on 12/01/2006 is acknowledged. The applicants have elected diabetic retinopathy from the disclosed species of diseases recited in Claim 4 and the compound N-{4- [2-(4-{[amino(imino)methyl] amino } phenyl)ethyl] -5 - [4-(methylsulfonyl)benzyl] - 1,3-thiazol-2-yl} acetamide from the disclosed species of compounds from Claims 5, 6 and 7. The restriction election has been made with traverse.

Applicants' argue that the diseases listed in claim 4 are characterized by increased vascular permeability and the present invention is directed to methods of treating such conditions and hence would not impose a serious burden on the office. The applicant's argument is not persuasive. In fact, it would impose a serious burden on the examiner to do a search to find out whether the elected species is used in the method of treatment of every single disease listed in claim 4. Thus the restriction requirement elected is made final. Claims 1-10 are pending.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 4-10 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims of 24, 26, 29, 30-33, 37, 38, 42 of copending Application No. 11/505321. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant application teaches a method of treating a vascular hyperpermeable disease (except macular edema) and the copending application teaches a method of treating all VAP-1 associated diseases.

The instant application (claims1, 4-10) is directed to a method of treating vascular hyperpermeable disease such as diabetic retinopathy, comprising administering a vascular adhesion protein-1 (VAP-1) inhibitor. The elected species of the instant application is the compound N-{4- [2-(4- {[amino(imino)methyl] amino } phenyl)ethyl] -5 - [4-(methylsulfonyl)benzyl] - 1,3- thiazol-2-yl} acetamide. The copending application (claims 37, 38, 24-32, 42) teaches a method of treatment of VAP-1 associated disease such as retinopathy (in diabetes patients) comprising administering VAP-1 inhibitor compounds. The copending application (claim 42) further teaches a method of inhibiting VAP-1 or treating VAP-1 associated disease comprising administering the elected species of the instant application, N-{4- [2-(4- {[amino(imino)methyl] amino } phenyl)ethyl] -5 - [4-(methylsulfonyl)benzyl] - 1,3-thiazol-2-yl} acetamide. Hence it is obvious to treat diabetic retinopathy, a vascular permeable disease by administering a VAP-1 inhibitor as claimed in the instant application as the

copending application teaches a method to treat all vascular permeable disease by administering VAP-1 inhibitors.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while enabling for compounds A and B (specification, p 21, pages 246-250) does not reasonably provide enablement for any other VAP-1 inhibitor compound. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to the invention commensurate in scope with these claims.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to In re Wands, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Forman, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the

claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1) The nature of the Invention:

The rejected claim is drawn to a method of treatment of vascular hyperpermeable disease (except macular edema) comprising administering to a subject a vascular adhesion protein-1 (VAP-1) inhibitor.

(2) Breadth of the claims:

Claim 1 is broad as it is drawn to a method of treatment of vascular hyperpermeable disease (except macular edema) comprising administering to a subject a vascular adhesion protein-1 (VAP-1) inhibitor. The complex nature of the subject matter of this invention is greatly exacerbated by the breadth of the claim.

(3) Guidance of the Specification:

The guidance given by the specification for the method of treatment of vascular hyperpermeable disease (except macular edema) comprising administering to a subject a vascular adhesion protein-1 (VAP-1) inhibitor is limited to compounds A and B.

(4) Working Examples:

The specification provides examples for the method of treatment of vascular hyperpermeable disease (except macular edema) comprising administering to a subject a vascular adhesion protein-1 (VAP-1) inhibitor is limited to compounds A and B (specification, pages 246-250).

(5) The relative skill of those in the art:

The relative skill of those in the medical treatment art is high, requiring advanced education and training.

(6) The predictability of art:

Claim 1 s drawn to a method of treatment of vascular hyperpermeable disease (except macular edema) comprising administering to a subject a vascular adhesion protein-1 (VAP-1) inhibitor. The claim is so broad and there is a high degree of unpredictability involved. Despite the advanced training in the medical treatment arts, the arts are highly unpredictable.

(7) The Quantity of Experimentation Necessary:

In order to practice the above claimed invention, one of skill in the art would have to first envision formulation, dosage, duration, route and, in the case of human treatment, an appropriate animal model system to test all the VAP-1 inhibitor compounds to determine whether or not they are useful in the treatment of vascular hyperpermeable disease. If unsuccessful, one of skill in the art would have to envision a modification in the formulation, dosage, duration, route of administration etc. and appropriate animal model system, or envision an entirely new combination of the above and test the system again. Therefore, it would require undue, unpredictable experimentation to practice the claimed invention of comprising administering every single VAP-1 inhibitor compound for the treatment of vascular hyperpermeable disease. Genetech, 108 F.3d at 1366 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent

protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while enabling for 1) inhibitory effect on VAP-1 enzyme activity in human and rat plasma (in vitro studies) by compound A 2) ocular permeability in diabetic rats by compounds A and B 3) increased retinal VAP-1 activity in diabetic rats from the effect of eye-drop instillation with compound A 4) increased retinal VEGF (vascular endothelial growth factor) level in diabetic rats with compound A (specification, p 21, pages 246-250) does not reasonably provide enablement for all the vascular permeable diseases. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to the invention commensurate in scope with these claims.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to In re Wands, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Forman, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1) The nature of the Invention:

The rejected claim is drawn to a method of treatment of vascular hyperpermeable disease (except macular edema) comprising administering to a subject a vascular adhesion protein-1 (VAP-1) inhibitor.

(2) Breadth of the claims:

Claim 1 is broad as it is drawn to a method of treatment of vascular hyperpermeable disease (except macular edema) comprising administering to a subject a vascular adhesion protein-1 (VAP-1) inhibitor. The complex nature of the subject matter of this invention is greatly exacerbated by the breadth of the claim.

(3) Guidance of the Specification:

The guidance given by the specification for the method of treatment of vascular hyperpermeable disease (except macular edema) comprising administering to a subject a vascular adhesion protein-1 (VAP-1) inhibitor is limited to the following data: 1) inhibitory effect of compound A on VAP-1 enzyme activity in human and rat plasma (in vitro studies) 2) compounds A and B on ocular permeability in diabetic rats 3) effect of eye-drop instillation with compound A on increased retinal VAP-1 activity in diabetic rats 4) effect of compound A on increased retinal VEGF (vascular endothelial growth factor) level in diabetic rats.

(4) Working Examples:

The specification provides a method of treatment of vascular hyperpermeable disease (except macular edema) comprising administering to a subject a vascular adhesion protein-1 (VAP-1) inhibitor with compounds A and B with the following examples: 1) inhibitory effect of compound A on VAP-1 enzyme activity in human and rat plasma (in vitro studies) 2) compounds A and B on ocular permeability in diabetic rats 3) effect of eye-drop instillation with compound A on increased retinal VAP-1 activity in diabetic rats 4) effect of compound A on increased retinal VEGF (vascular endothelial growth factor) level in diabetic rats (specification, pages 246-250).

(5) The relative skill of those in the art:

The relative skill of those in the medical treatment art is high, requiring advanced education and training.

(6) The predictability of art:

Claim 1 is drawn to a method of treatment of vascular hyperpermeable disease (except macular edema) comprising administering to a subject a vascular adhesion protein-1 (VAP-1) inhibitor. The claim is so broad and there is a high degree of unpredictability involved. Despite the advanced training in the medical treatment arts, the arts are highly unpredictable.

(7) The Quantity of Experimentation Necessary:

In order to practice the above claimed invention, one of skill in the art would have to first envision formulation, dosage, duration, route and, in the case of human treatment, an appropriate animal model system to test all the VAP-1 inhibitor

compounds for all the vascular hyperpermeable diseases. If unsuccessful, one of skill in the art would have to envision a modification in the formulation, dosage, duration, route of administration etc. and appropriate animal model system, or envision an entirely new combination of the above and test the system again. Therefore, it would require undue, unpredictable experimentation to practice the claimed invention of comprising administering every single VAP-1 inhibitor compound for the treatment of all vascular hyperpermeable disease. Genetech, 108 F.3d at 1366 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 - 4 are rejected under 35 U.S.C. 102(b) as being anticipated by Garpenstand et al (Diabet Med, 1999, Jun 16(6), 514-21).

Garpenstand et al teaches the use of a potent and specific inhibitor of human semicarbazide-sensitive amine oxidase (SSAO) (Vascular adhesion protein –1) in the prevention of retinopathy in Type I and Type 2 diabetes mellitus (p 514 conclusions, p 520 lines 3-7).

Claims 1 and 4 are rejected under 35 U.S.C. 102(b) as being anticipated by Smith et al. (WO 02/02541).

Smith et al. teaches that SSAO, Vascular adhesion Protein (VAP-1) inhibitors are useful in the treatment of inflammatory bowel diseases, chronic skin dermatoses, and

vascular diseases such as atherosclerosis, vascular retinopathies, and neuropathies such as polyneuropathy, mononeuropathy, and autonomic neuropathy (see abstract, p 8, lines 17-22).

Claim Rejections - 35 USC § 102

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 4, 5-10 are rejected under 35 U.S.C. 102(e) as being anticipated by Inoue et al (U.S. 7,125,901). The reference teaches that VAP-1 inhibitors are useful in the treatment of VAP-1 associated disease (col. 2, lines 62-65). The reference further teaches the elected species N-{4- [2-(4- {[amino(imino)methyl] amino } phenyl)ethyl] -5 - [4-(methylsulfonyl)benzyl] -1,3-thiazol-2-yl} acetamide and also the compound N-{4-[2-(4 - { [amino (imino)methyl] amino } phenyl)ethyl] - 1,3-thiazol-2-yl } acetamide (in claim 10 of the instant application) as a VAP-1 inhibitor, and the use of such compounds in the treatment of VAP-1 associated disease such as retinopathy (in diabetes patients) (col. 6, lines 3-27).

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). (The effective filing date of the application is 3/31/2003 and the effective filing date of the reference is 1/27/2003). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention

disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Conclusion

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Umamaheswari Ramachandran whose telephone number is 571-272-9926. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER